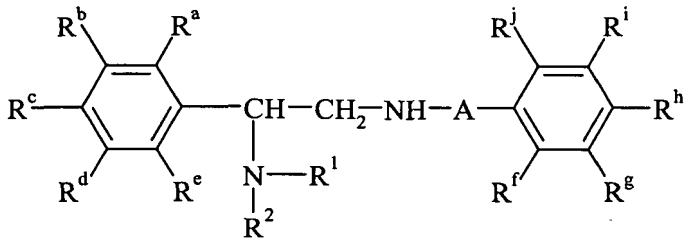
Patent Claims

1. A Method of treatment and/or prevention of a disease wherein the activity of a CCR3 receptor is involved, comprising administering to a mammal in need of such treatment a therapeutically effective amount of a 1-phenyl-1,2-diaminoethane derivative of formula (I)



(I),

wherein

R^a through R^e each independently represent a hydrogen or halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl $-NH_2$, $-NH(C_1$-C_4-alkyl), $-N(C_1$-C_4-alkyl)$_2$ and phenyl, wherein any of these groups are optionally substituted by one or more of the groups hydroxy, halogen, CF_3, or

two adjacent groups R^a and R^b or R^b and R^c together form a group $-O-(CH_2)_m-O-$, $-(CH_2)_n-$ or $-CH=CH-CH=CH-$, in which m is 1 or 2, and n is 3, 4 or 5;

R^f through R^j each independently represent a hydrogen or halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl, cyano, $-NH_2$, $-NH(C_1$-C_4-alkyl), $-N(C_1$-C_4-alkyl)$_2$, wherein any of these groups are optionally substituted by one or more hydroxy or halogen groups,

R^1 and R^2 each independently represent a hydrogen atom or a group selected from C_1-C_6-alkyl, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl, piperidinyl and phenyl, wherein any of these groups optionally are optionally substituted by one or more of the groups C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, hydroxy, halogen, C_3-

C_8-cycloalkyl, , pyridyl, piperidyl, pyrrolidinyl, oxopyrrolidinyl, tetrahydrofuranyl, furanyl, phenyl, hydroxyphenyl, alkoxyphenyl, dialkoxyphenyl, methylendioxyphenyl, CF_3, or $-NR_3R_4$, in which R_3 and R_4 each independently represent hydrogen, C_1-C_6-alkyl, C_1-C_4-alkanoyl, C_3-C_6-cycloalkylmethyl, omega-hydroxy-C_2-C_4-alkyl, 1,3-dihydroxyprop-2-yl

R^1 and R^2 together with the interjacent nitrogen atom form a a 5- to 7-membered, saturated or unsaturated heterocyclic group, which optionally contain one or two hetero atoms selected from among oxygen, nitrogen or sulphur, wherein said heterocyclic group are optionally substituted by hydroxy, C_1-C_4-alkyl, C_3-C_8-cycloalkyl, C_3-C_6-cycloalkylmethyl, hydroxy-C_3-C_8-cycloalkyl, C_1-C_4-alkoxy, C_1-C_4-alkoxycarbonyl, 2-oxobenzimidazolyl, piperidyl, benzyl 9-H-fluorenyl, di-(C_1-C_4-alkyl)-amino-C_1-C_4-alkyl or $-NR_3R_4$, in which R_3 and R_4 each independently represent hydrogen, C_1-C_6-alkyl, C_1-C_4-alkanoyl, C_3-C_6-cycloalkylmethyl, omega-hydroxy-C_2-C_4-alkyl, 1,3-dihydroxyprop-2-yl, or a group of formula

$$-(CH_2)_n\text{-phenyl},$$

in which n is 0 or an integer from 1 to 3, and
the phenyl group is optionally substituted by one to three substituents selected from the group the group consisting of C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl, $-NH_2$, $-NH(C_1\text{-}C_4\text{-alkyl})$, $-N(C_1\text{-}C_4\text{-alkyl})_2$,

wherein any of said substituents are optionally substituted by one or more hydroxy or halogen groups), and

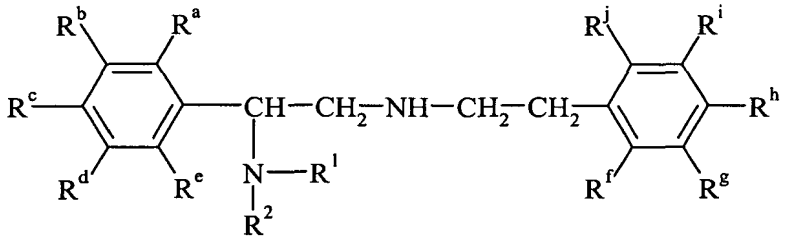
wherein said heterocyclic group is optionally fused with one or two benzene rings; and

A represents $-CH_2CH_2-$, -C(=O)-NH- or $-C(=O)-CH_2-$;

optionally in the form of their tautomers, racemates, enantiomers, diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition salts thereof.

2. The Method according to claim 1, wherein the disease is selected from allergic rhinits, atopic dermatitis, inflammatory bowel disease, idiopathic pulmonary fibrosis, bullous pemphigoid, helminthic parasitic infections, allergic colitis, eczema, conjunctivitis, transplantation, familial eosinophilia, eosinophilic cellulitis, pneumonias, eosinophilic fasciitis, eosinophilic gastroenteritis, drug induced eosinophilia, HIV infection, cystic fibrosis, Churg-Strauss syndrome, lymphoma, Hodgkin's disease, colonic carcinoma, COPD and asthma.

3. A 1-phenyl-1,2-diaminoethane derivative of formula (IA)



(IA),

wherein

R^a through R^e each independently represent a hydrogen or halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl $-NH_2$, $-NH(C_1$-C_4-alkyl), $-N(C_1$-C_4-alkyl)$_2$ and phenyl, wherein any of these groups are optionally substituted by one or more of the groups hydroxy, halogen, CF_3, or

two adjacent groups R^a and R^b or R^b and R^c together form a group $-O-(CH_2)_m-O-$, $-(CH_2)_n-$ or $-CH=CH-CH=CH-$, in which m is 1 or 2, and n is 3, 4 or 5;

R^f through R^j each independently represent a hydrogen or halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl, cyano, -NH_2, -NH(C_1-C_4-alkyl),-N(C_1-C_4-alkyl)$_2$, wherein any of these groups are optionally substituted by one or more hydroxy or halogen groups,

R^1 and R^2 each independently represent a hydrogen atom or a group selected from C_1-C_6-alkyl, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl, and phenyl, wherein any of these groups optionally are substituted by one or more of the groups C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, hydroxy, halogen, C_3-C_8-cycloalkyl, -NH_2, -NH(C_1-C_4-alkyl), -N(C_1-C_4-alkyl)$_2$, -N(C_1-C_4-alkanoyl)(C_1-C_4-alkyl), pyridyl, piperidyl, pyrrolidinyl, oxopyrrolidinyl, tetrahydrofuranyl, furanyl, phenyl, hydroxyphenyl, alkoxyphenyl, dialkoxyphenyl, methylendioxyphenyl, CF_3, or

R^1 and R^2 together with the interjacent nitrogen atom form a a 5- to 7-membered, saturated or unsaturated heterocyclic group, which optionally contain one or two hetero atoms selected from among oxygen, nitrogen or sulphur, wherein said heterocyclic group is optionally substituted by hydroxy, C_1-C_4-alkyl, C_3-C_8-cycloalkyl, C_3-C_6-cycloalkylmethyl, hydroxy-C_3-C_8-cycloalkyl, C_1-C_4-alkoxy, C_1-C_4-alkoxycarbonyl, 2-oxobenzimidazolyl, piperidyl, benzyl 9-H-fluorenyl, di-(C_1-C_4-alkyl)-amino-C_1-C_4-alkyl or -NR_3R_4, in which R_3 and R_4 each independently represent hydrogen, C_1-C_6-alkyl, C_1-C_4-alkanoyl, C_3-C_6-cycloalkylmethyl, omega-hydroxy-C_2-C_4-alkyl, 1,3-dihydroxyprop-2-yl, or a group of formula

$$-(CH_2)_n\text{-phenyl},$$

in which n is 0 or an integer from 1 to 3, and

the phenyl group is optionally substituted by one to three substituents selected from the group the group consisting of C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl, -NH_2, -NH(C_1-C_4-alkyl), -N(C_1-C_4-alkyl)$_2$,

wherein any of said substituents are optionally substituted by one or more hydroxy or halogen groups), and

wherein said heterocyclic group is optionally fused with one or two benzene rings; optionally in the form of their tautomers, racemates, enantiomers, diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition salts thereof.

4. The 1-phenyl-1,2-diaminoethane derivative of formula (IA) according to claim 3, wherein

R^1 and R^2 together with the interjacent nitrogen atom form a 5- to 7-membered, saturated or unsaturated heterocyclic group, which optionally contain one or two hetero atoms selected from among oxygen, nitrogen or sulphur, wherein said heterocyclic group is optionally substituted by hydroxy, C_1-C_4-alkyl, C_3-C_8-cycloalkyl, hydroxy-C_3-C_8-cycloalkyl, C_1-C_4-alkoxycarbonyl, phenyl, alkoxyphenyl, halophenyl, trifluoromethylphenyl, 2-oxobenzimidazolyl, piperidyl, benzyl 9-H-fluorenyl or di-(C_1-C_4-alkyl)-amino-C_1-C_4-alkyl, and which is optionally fused with one or two benzene rings;

5. The 1-phenyl-1,2-diaminoethane derivative of formula (IA) according to claim 4, wherein

R^a R^b, R^d and R^e each represent a hydrogen atom;

R^c represents a hydrogen or halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl $-NH_2$, $-NH(C_1$-C_4-alkyl), $-N(C_1$-C_4-alkyl)$_2$ and phenyl, wherein any of these groups are optionally substituted by one or more of the groups hydroxy, halogen, CF_3, or

R^f represents a hydrogen atom or a C_1-C_4-alkoxy group,

R^g and R^i each independently represent a hydrogen or halogen atom or a C_1-C_6-alkyl group optionally substituted by halogen,

R^h represents a hydrogen or halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl, cyano ,
$-NH_2$, $-NH(C_1$-C_4-alkyl), $-N(C_1$-C_4-alkyl$)_2$, wherein any of these groups are optionally substituted by one or more of the groups hydroxy or halogen,

R^j represents a hydrogen atom,

R^1 and R^2 together with the interjacent nitrogen atom form a piperidine or piperazine group, which is optionally substituted by hydroxy, C_1-C_4-alkyl, C_3-C_8-cycloalkyl, hydroxy-C_3-C_8-cycloalkyl, C_1-C_4-alkoxycarbonyl, phenyl, alkoxyphenyl, halophenyl, trifluoromethylphenyl, 2-oxobenzimidazolyl, piperidyl, benzyl 9-H-fluorenyl or di-(C_1-C_4-alkyl)-amino-C_1-C_4-alkyl, and which is optionally fused with one or two benzene rings;

optionally in the form of their tautomers, racemates, enantiomers, diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition salts thereof.

6. The 1-phenyl-1,2-diaminoethane derivative of formula (IA) according to claim 5, wherein

R^a R^b, R^d and R^e each represent a hydrogen atom;

R^c represents a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_3-C_8-cycloalkyl and phenyl, wherein any of these groups are optionally substituted by one or more of the groups hydroxy, halogen, CF_3,

R^f represents a hydrogen atom or a methoxy group,

R^g and R^i each independently represent a hydrogen or chlorine atom or a methyl group,

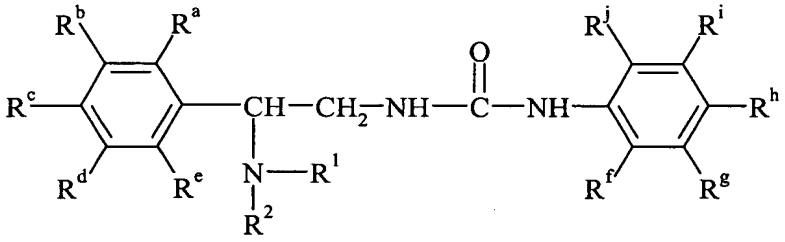
R^h represents a hydrogen or chlorine atom or a group selected from methyl, *tert*-butyl, trifluoromethyl, methoxy, cyano, amino and dimethylamine;

R^j represents a hydrogen atom,

R^1 and R^2 together with the interjacent nitrogen atom form a piperidine or piperazine group, which are optionally substituted by cyclohexyl or phenyl,

optionally in the form of their tautomers, racemates, enantiomers, diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition salts thereof.

7. A 1-phenyl-1,2-diaminoethane derivative of formula (IB)



(IB),

wherein

R^a through R^e each independently represent a hydrogen or halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl $-NH_2$, $-NH(C_1$-C_4-alkyl), $-N(C_1$-C_4-alkyl)$_2$ and phenyl, wherein any of these groups are optionally substituted by one or more of the groups hydroxy, halogen, CF_3, or

two adjacent groups R^a and R^b or R^b and R^c together form a group $-O-(CH_2)_m-O-$, $-(CH_2)_n-$ or $-CH=CH-CH=CH-$, in which m is 1 or 2, and n is 3, 4 or 5;

R^f through R^j each independently represent a hydrogen or halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-

alkinyl, C_3-C_8-cycloalkyl, cyano, amino, -N(C_1-C_4-alkyl)$_2$, wherein any of these groups are optionally substituted by one or more hydroxy groups,

provided that at least one of the groups R^b, R^c, R^d, R^g, R^h and R^j is different from hydrogen;

R^1 and R^2 each independently represent a hydrogen atom or a group selected from C_1-C_6-alkyl, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl, and phenyl, wherein any of these groups optionally are substituted by one or more of the groups C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, hydroxy, halogen, C_3-C_8-cycloalkyl, -NH_2, -NH(C_1-C_4-alkyl), -N(C_1-C_4-alkyl)$_2$, -N(C_1-C_4-alkanoyl)(C_1-C_4-alkyl), pyridyl, piperidyl, pyrrolidinyl, oxopyrrolidinyl, tetrahydrofuranyl, furanyl, phenyl, hydroxyphenyl, alkoxyphenyl, dialkoxyphenyl, methylendioxyphenyl, CF_3, or

R^1 and R^2 together with the interjacent nitrogen atom form a a 5- to 7-membered, saturated or unsaturated heterocyclic group, which optionally contain one or two hetero atoms selected from among oxygen, nitrogen or sulphur, wherein said heterocyclic group is optionally substituted by hydroxy, C_1-C_4-alkyl, C_3-C_8-cycloalkyl, C_3-C_6-cycloalkylmethyl, hydroxy-C_3-C_8-cycloalkyl, C_1-C_4-alkoxy, C_1-C_4-alkoxycarbonyl, 2-oxobenzimidazolyl, piperidyl, benzyl 9-H-fluorenyl, di-(C_1-C_4-alkyl)-amino-C_1-C_4-alkyl or -NR_3R_4, in which R_3 and R_4 each independently represent hydrogen, C_1-C_6-alkyl, C_1-C_4-alkanoyl, C_3-C_6-cycloalkylmethyl, omega-hydroxy-C_2-C_4-alkyl, 1,3-dihydroxyprop-2-yl, or a group of formula

-$(CH_2)_n$-phenyl,

in which n is 0 or an integer from 1 to 3, and

the phenyl group is optionally substituted by one to three substituents selected from the group the group consisting of C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl, -NH_2, -NH(C_1-C_4-alkyl), -N(C_1-C_4-alkyl)$_2$,

wherein any of said substituents are optionally substituted by one or more hydroxy or halogen groups), and

wherein said heterocyclic group is optionally fused with one or two benzene rings;

optionally in the form of their tautomers, racemates, enantiomers, diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition salts thereof.

8. The 1-phenyl-1,2-diaminoethane derivative of formula (IB) according to claim 7, wherein

R^1 and R^2 together with the interjacent nitrogen atom form a 5- to 7-membered, saturated or unsaturated heterocyclic group, which optionally contain one or two hetero atoms selected from among oxygen, nitrogen or sulphur, substituted by hydroxy, C_1-C_4-alkyl, C_3-C_8-cycloalkyl, hydroxy-C_3-C_8-cycloalkyl, C_1-C_4-alkoxycarbonyl, phenyl, alkoxyphenyl, halophenyl, trifluoromethylphenyl, 2-oxobenzimidazolyl, piperidyl, benzyl 9-H-fluorenyl or di-(C_1-C_4-alkyl)-amino-C_1-C_4-alkyl, and which is optionally fused with one or two benzene rings.

9. The 1-phenyl-1,2-diaminoethane derivative of formula (IB) according to claim 8, wherein

R^a R^b, R^d and R^e each represent a hydrogen atom;

R^c represents a atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl -NH_2, -NH(C_1-C_4-alkyl), -N(C_1-C_4-alkyl)$_2$ and phenyl, wherein any of these groups are optionally substituted by one or more of the groups hydroxy, halogen, CF_3, or

R^f represents a hydrogen atom or a C_1-C_4-alkoxy group,

R^g and R^i each independently represent a hydrogen or halogen atom or a C_1-C_6-alkyl group,

R^h represents a hydrogen or halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, C_2-C_6-alkenyl C_2-C_6-alkinyl, C_3-C_8-cycloalkyl, cyano, amino or -N(C_1-C_4-alkyl)$_2$, wherein any of these groups are optionally substituted by one or more of the groups hydroxy,

R^j represents a hydrogen atom,

R^1 and R^2 together with the interjacent nitrogen atom form a piperidine group, which is optionally substituted by hydroxy, C_1-C_4-alkyl, C_3-C_8-cycloalkyl, hydroxy-C_3-C_8-cycloalkyl, C_1-C_4-alkoxycarbonyl, phenyl, alkoxyphenyl, halophenyl, trifluoromethylphenyl, 2-oxobenzimidazolyl, piperidyl, benzyl 9-H-fluorenyl or di-(C_1-C_4-alkyl)-amino-C_1-C_4-alkyl, and which is optionally fused with one or two benzene rings;

optionally in the form of their tautomers, racemates, enantiomers, diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition salts thereof.

10. The 1-phenyl-1,2-diaminoethane derivative of formula (IB) according to claim 9, wherein

R^a R^b, R^d and R^e each represent a hydrogen atom;

R^c represents a halogen atom or a group selected from C_1-C_6-alkyl, C_1-C_4-alkoxy, C_3-C_8-cycloalkyl and phenyl, wherein any of these groups are optionally substituted by one or more of the groups hydroxy, halogen, CF_3,

R^f represents a hydrogen atom or a methoxy group,

R^g and R^i each independently represent a hydrogen or chlorine atom or a methyl group,

R^h represents a hydrogen or chlorine atom or a group selected from methyl, *tert*-butyl, trifluoromethyl, methoxy, cyano, amino and dimethylamino;

R^j represents a hydrogen atom,

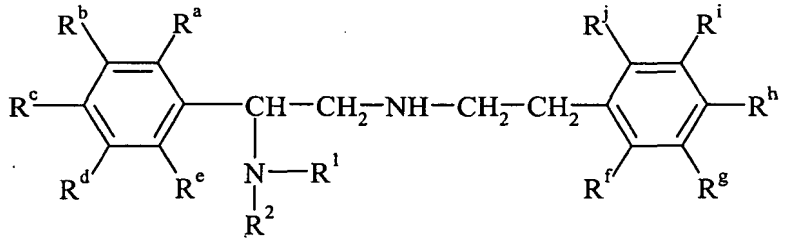
R^1 and R^2 together with the interjacent nitrogen atom form a piperidine group, which is optionally substituted by cyclohexyl or phenyl,

optionally in the form of their tautomers, racemates, enantiomers, diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition salts thereof.

11. A Method of prevention and/or treatment of diseases wherein CCR3 activity modulators have a therapeutic benefit comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of formula (IA) or formula (IB) as in any one of claims 3-10.

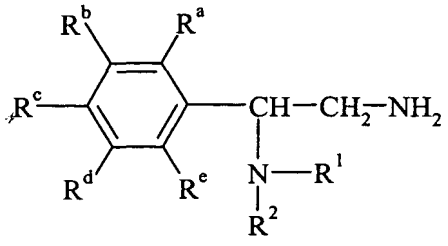
12. A Pharmaceutical composition comprising a therapeutically effective amount of one or more compounds of formulae (IA or (IB) as in any one of claims 3-10.

13. A Process for preparing compounds of general formula (IA)



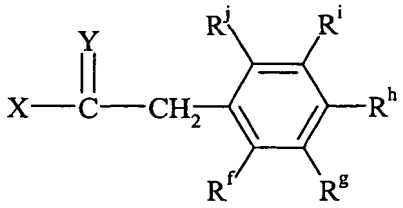
(IA),

wherein the groups R^1, R^2 and R^a through R^j have the meanings given in claims 3 to 6, characterized in that a compound of formula (IIA)



(IIA),

wherein the groups R^1, R^3 and R^a through R^e have the meanings given in claims 3 to 6, is reacted with a compound of formula (IIIA)



(IIIA),

wherein the groups R^f through R^j have the meanings given in claims 3 to 6,

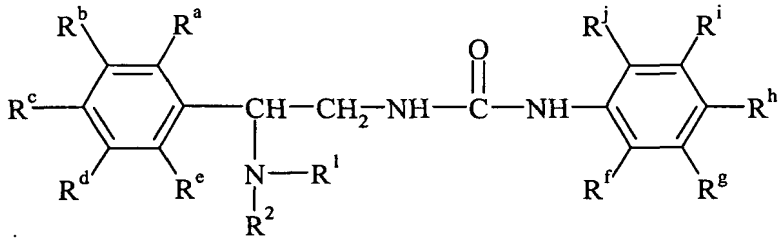
(a) X represents hydroxy or a leaving group and Y represents two hydrogen atoms an oxygen atom, or

(b) X represents a hydrogen atom and Y represents an oxygen atom,

in a nucleophilic substitution for type (a) optionally followed by reduction for X = OH or a leaving group, or

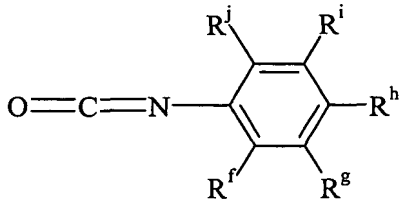
in a reductive amination for type (b).

14. A Process for preparing compounds of general formula (IB)



(IB),

wherein the groups R^1, R^2 and R^a through R^j have the meanings given in claims 7 to 10, characterized in that a compound of formula (IIA) according to claim 13, is reacted with a compound of formula (IIIB)



(IIIA),

wherein the groups R^f through R^j have the meanings given in claims 7 to 10.